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Update [1/26/2023] The U.S. Food and Drug Administration today revised the Emergency Use Authorization (/media/154704/download?attachment) (EUA) for Evusheld (tixagevimab co-packaged with cilgavimab) to limit its use to when the combined frequency of non-susceptible SARS-CoV-2 variants nationally is less than or equal to 90%. Based on this revision, **Evusheld is not currently authorized for use in the U.S. until further notice by the Agency.**

Data show Evusheld is unlikely to be active against certain SARS-CoV-2 variants. According to the most recent CDC Nowcast data (https://covid.cdc.gov/covid-data-tracker/), these variants are projected to be responsible for more than 90% of current infections in the U.S. This means that Evusheld is not expected to provide protection against developing COVID-19 if exposed to those variants.

Today's action to limit the use of Evusheld prevents exposing patients to possible side effects of Evusheld such as allergic reactions, which can be potentially serious, at a time when fewer than 10% of circulating variants in the U.S. causing infection are susceptible to the product.

Monoclonal antibodies are laboratory-made proteins that mimic the immune system's ability to fight off harmful pathogens such as viruses, like SARS-CoV-2. And like other viruses, SARS-CoV-2 can mutate over time, resulting in certain products not working against certain variants. This is the case with Evusheld and prompted the changes to the authorization that FDA is making today.

Should a patient become infected with SARS-CoV-2 and develop symptoms of COVID-19, they should seek medical attention, including starting treatment for COVID-19 as appropriate. There are several treatments (/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization#coviddrugs) – Paxlovid, Veklury (remdesivir) and Lagevrio (molnupiravir) – that are expected to work against currently circulating variants, and that are authorized or approved to treat certain patients with mild-to-moderate COVID-19 who are at high risk for progression to severe disease, including hospitalization or death. Healthcare providers should assess whether treatments are right for their patients.

The U.S. Government recommends that facilities and providers with Evusheld retain all product in the event that SARS-CoV-2 variants which are neutralized by Evusheld become more prevalent in the U.S. in the future. Retained product must be appropriately held in accordance with storage conditions detailed in the authorized Fact Sheet for Health Care Providers (/media/154701/download?attachment) and the Letter of Authorization (/media/154704/download?attachment).

FDA will continue to work with ASPR, the CDC, and the National Institutes of Health on surveillance of variants that may impact the use of the therapies authorized for emergency use. We will provide further updates and consider additional action as new information becomes available. Any updates will be made available on FDA's website (/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization#coviddrugs).

FDA releases important information about risk of COVID-19 due to certain variants not neutralized by Evusheld

Update [1/6/2023] FDA is closely monitoring the emergence of the XBB.1.5 subvariant, a SARS-CoV-2 Omicron variant that is currently estimated (https://covid.cdc.gov/covid-data-tracker/#variant-proportions) to account for 28% of circulating variants in the U.S. Because of its similarity to variants that are not neutralized by Evusheld (e.g., XBB), FDA does not anticipate that Evusheld will neutralize XBB.1.5. This means that Evusheld may not provide protection against developing COVID-19 for individuals who have received Evusheld and are later exposed to XBB.1.5. However, we are awaiting additional data to verify that Evusheld is not active against XBB.1.5. We will provide further updates as new information becomes available.

Health care providers should inform individuals of the increased risk, compared to other variants, for COVID-19 due to SARS-CoV-2 variants not neutralized by Evusheld.

If signs and symptoms of COVID-19 occur, advise individuals to test for COVID-19 and seek medical attention, including starting treatment for COVID-19 as appropriate.

Update [10/3/2022] FDA added important information to the authorized Fact Sheets for Evusheld (tixagevimab co-packaged with cilgavimab) to inform health care providers and individuals receiving Evusheld of the increased risk for developing COVID-19 when exposed to variants of SARS-CoV-2 that are not neutralized by Evusheld. Detailed neutralization data can be found in the revised authorized **Fact Sheet for Healthcare Providers**.

(/media/154701/download) Health care professionals should inform patients of this risk and advise patients who develop signs or symptoms of COVID-19 to test for SARS-CoV-2 infection and promptly seek medical attention, including starting treatment for COVID-19, as appropriate if they test positive.

Evusheld is currently the only option for pre-exposure prophylaxis (PrEP) of COVID-19 and is authorized under **Emergency Use Authorization (/media/154704/download)** (EUA) for use in immunocompromised individuals who may not mount an adequate response to COVID-19 vaccination, and for individuals for whom COVID-19 vaccination is not recommended due to a history of a severe adverse reaction. It is authorized to be administered every six months. Use of Evusheld is not a substitute for COVID-19 vaccination, and individuals for whom COVID-19 vaccination is recommended should get vaccinated. Individuals who received Evusheld but who develop COVID-19 remain eligible for use of any of the available treatments for COVID-19 if the criteria for use are met.

FDA continues to recommend Evusheld as an appropriate option for PrEP to prevent COVID-19, in combination with other preventative measures like getting vaccinated and boosted as recommended, as Evusheld still offers protection against many of the currently circulating variants and may offer protection against future variants.

What Patients Should Know:

- Talk with your health care provider about appropriate treatment options in case you develop COVID-19. There are several approved and authorized treatments for COVID-19 that are expected to retain activity against currently circulating SARS-CoV-2 variants.
- If you develop COVID-19 symptoms, tell your health care provider and test right away. It's not possible to know which variant of SARS-CoV-2 you may have contracted. Timely treatment can reduce your risk of developing severe disease, including decreasing your risk of hospitalization or death.
- If recommended by your health care provider, get vaccinated or boosted with a bivalent booster dose to help your body increase your protection against SARS-CoV-2 infection. Follow CDC's guidelines (https://www.cdc.gov/coronavirus/2019-ncov/prevent-getting-sick/prevention.html) on additional prevention strategies to protect yourself from getting sick.

What Health Care Providers Should Know:

- Prescribers should monitor CDC regional variant frequency data (https://covid.cdc.gov/covid-data-tracker/#variant-proportions) and refer to the table of variants detailed in the Fact Sheet for Health Care Providers (/media/154701/download) for the latest data on the neutralization activity of Evusheld

against SARS-CoV-2 variants in your area. Prescribers should discuss the risk of developing COVID-19 infection with patients receiving Evusheld.

- There are several treatments (/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization#coviddrugs) – Paxlovid, Veklury (remdesivir), bebtelovimab, and Lagevrio (molnupiravir) – that are expected to retain activity against currently circulating variants, and that are authorized or approved to treat certain patients with mild-to-moderate COVID-19 who are at high risk for progression to severe disease, including hospitalization or death. Health care providers should assess whether these treatments are right for their patient in the event the patient develops mild-to-moderate COVID-19.
- FDA has also updated the list of medical conditions or treatments that may result in moderate to severe immune compromise. The conditions listed in the Fact Sheet for Health Care Providers (/media/154701/download) are not intended to be an all-inclusive list. Patients with other conditions not listed may also have moderate to severe immune compromise and therefore be eligible for Evusheld therapy, assuming the remaining terms and conditions of the authorization are met.

FDA authorizes revisions to Evusheld dosing

Update [6/29/2022] There are different variants (and subvariants) of SARS-CoV-2, and FDA continues to evaluate how well Evusheld (tixagevimab co-packaged with cilgavimab) neutralizes them. Currently, the Omicron BA.2, BA.2.12.1, BA.4, and BA.5 subvariants are circulating in the United States. Nonclinical data and pharmacokinetic modeling suggest that activity against these subvariants may be retained for six months at drug concentrations achieved following an Evusheld dose of 300 mg of tixagevimab and 300 mg cilgavimab.

Therefore, on June 29, 2022, FDA revised the Evusheld Fact Sheet for Healthcare Providers (/media/154701/download) to recommend repeat dosing every six months with a dose of 300 mg of tixagevimab and 300 mg cilgavimab if patients need ongoing protection. The previous Fact Sheet for Healthcare Providers did not provide a specific recommendation on the dosing interval.

We continue to monitor the neutralizing activity of Evusheld against emerging SARS-CoV-2 variants and will provide additional updates as needed.

For further details please refer to the Frequently Asked Questions for Evusheld. (/media/154703/download)

[2/24/2022] The U.S. Food and Drug Administration has revised the emergency use authorization for Evusheld (tixagevimab co-packaged with cilgavimab) (/media/154704/download) to change the initial dose for the authorized use as pre-exposure prophylaxis (prevention) of COVID-19 in certain adults and pediatric patients.
Based on the most recent information and data available, Evusheld may be less active against certain Omicron subvariants. The dosing regimen was revised because available data indicate that a higher dose of Evusheld may be more likely to prevent infection by the COVID-19 Omicron subvariants BA.1 and BA.1.1 than the originally authorized Evusheld dose.

Previously, the authorized Evusheld dosage was 150 mg of tixagevimab and 150 mg of cilgavimab administered as two separate consecutive intramuscular injections, with repeat doses every six months while SARS-CoV-2 remains in circulation. With this EUA revision, FDA has increased the initial authorized dose to 300 mg of tixagevimab and 300 mg of cilgavimab. Patients who have already received the previously authorized dose (150 mg of tixagevimab and 150 mg of cilgavimab) should receive an additional dose of 150 mg of tixagevimab and 150 mg of cilgavimab as soon as possible to raise their monoclonal antibody levels to those expected for patients receiving the higher dose.

Evusheld is authorized for the emergency use as pre-exposure prophylaxis (PrEP) for prevention of COVID-19 in certain adults and pediatric patients (12 years of age and older weighing at least 40 kg). Health care providers should only administer it to individuals who are not currently infected with SARS-CoV-2 and who have not had a known recent exposure to someone infected with SARS-CoV-2. Evusheld is only authorized for those:

- who have moderate-to-severe immune compromise due to a medical condition or who have received immunosuppressive medications or treatments and may not mount an adequate immune response to COVID-19 vaccination or
- for whom vaccination with any available approved or authorized COVID-19 vaccine is not recommended due to a history of severe adverse reaction (e.g., severe allergic reaction) to a COVID-19 vaccine(s) and/or COVID-19 vaccine component(s).

The duration of protection provided by Evusheld against symptomatic SARS-CoV-2 infection may not be as long as was shown in the clinical trial supporting the initial authorization because the clinical trial data came from a time period before the emergence of the BA.1 and BA.1.1 subvariants. However, it is not known whether BA.1 and BA1.1 will still be circulating in the coming months or whether another Omicron subvariant, BA.2, for which Evusheld is expected to have greater neutralizing activity, will become dominant. Because it is unclear which SARS-CoV-2 variant or Omicron subvariant will become dominant in the United States over the next few months, the recommended timing for repeat dosing cannot be provided at

this time. We will continue to monitor the situation closely and will provide updates with redosing recommendations in the near future when more data are available to determine the appropriate timing of redosing (e.g., 3 months or 6 months after the prior dose).

What should patients know:

- Patients who previously received an initial lower dose of Evusheld (150 mg of tixagevimab and 150 mg of cilgavimab) should contact their health care provider and return for an additional 150 mg of tixagevimab and 150 mg of cilgavimab dose as soon as possible. Any subsequent repeat dosing will be timed from the date of this additional Evusheld dose.
- Patients who have not received any doses of Evusheld should talk to their health care provider to determine whether, based on their individual circumstances, they are eligible to receive it. If they are eligible, they should receive the 300 mg of tixagevimab and 300 mg of cilgavimab dose.
- Patients with any additional questions should contact their health care provider.

What health care professionals should know:

- Health care professionals should contact patients who received the previously authorized Evusheld dose to return for an additional 150 mg tixagevimab and 150 mg cilgavimab dose as soon as possible.
- The volume of each injection for the new, higher dose will be larger, 3 mL instead of 1.5 mL. This means that the injections should be limited to large muscles on the body that can accommodate this volume (e.g., the gluteal muscles).
- Health care professionals should review the updated Fact Sheets and Dear Health Provider Letter for Evusheld.
- As part of the EUA, FDA requires health care providers who prescribe Evusheld to report all medication errors and serious adverse events considered to be potentially related to Evusheld through FDA's MedWatch Adverse Event Reporting program (/safety/medwatch-fda-safety-information-and-adverse-event-reporting-program). Providers can complete and submit the report online (https://www.accessdata.fda.gov/scripts/medwatch/index.cfm?action=reporting.home); or download and complete the form, then submit it via fax at 1-800-FDA-0178.